IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Patent Application of

Ivan PETYAEV — Atty. Ref.: 620-433

Serial No. 10/574,852 — TC/A.U.: 1623

Filed: April 6, 2006 — Examiner: Peselev

For: METHOD AND MEANS FOR MODULATING LIPID METABOLISM

* *

June 23, 2010

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPEAL BRIEF

Sir:

Applicant hereby appeals the final rejection of claims 12, 13, 21, 29 and 32-38, in the Office Action dated February 18, 2010, and submits the present Appeal Brief pursuant to 37 CFR § 41.37.

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(1) REAL PARTY IN INTEREST

The real PARTY IN INTEREST is CAMBRIDGE THERANOSTICS LIMITED, THE BABRAHAM RESEARCH CAMPUS, BABRAHAM, CAMBRIDGE, UNITED KINGDOM CB2 4AT, by way of an Assignment from the inventors, recorded in the U.S. Patent and Trademark Office on October 19, 2006, at Reel 08466, Frame 0467.

(2) RELATED APPEALS AND INTERFERENCES

The appellant, the appellant's legal representative, and the assignee are not aware of any related prior or pending appeals or interferences or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

(3) STATUS OF THE CLAIMS

Claims 12, 13, 21, 29 and 32-38 are pending.

Claims 12, 13, 21, 29 and 32-38 have been finally rejected.

The originally-filed claims 1-26 were amended, without prejudice, in a Preliminary Amendment filed April 6, 2006.

Claims 1-11 and 23-26 were canceled, claims 12 and 15 were amended, and new claims 27-28 added in an Amendment filed September 11, 2007. Claims 12-22, 27 and 28 were pending upon entry of the Amendment.

Claim 12 was further amended, claims 15, 27 and 28 canceled, and new claim 29 added in an Amendment After Final Rejection dated February 25, 2008. The Amendment After Final Rejection dated February 25, 2008 was entered upon filing of the Request for Continued Examination (RCE) on April 7, 2008. See page 2 of the Office Action dated April 24, 2008. Claims 12-14, 16-22 and 29 were pending upon entry of the Amendment After Final Rejection..

New claims 30-32 were added with an Amendment dated July 24, 2008. Claims 12-14, 16-22 and 29-32 were pending upon entry of the Amendment.

Claims 14, 16-20, 22, 30 and 31 were canceled, claims 33-38 newly presented and claims 12, 21 and 32 amended in an Amendment After Final Rejection filed January 23, 2009 which was entered with the filing of the RCE on January 23, 2009.

See page 2 of the Office Action dated February 12, 2009. Claims 12, 13, 21, 29 and 32-38 were pending upon entry of the Amendment After Final Rejection..

Claims 12, 13, 21, 29 and 32-38 are pending and the subject of the present appeal.

Claims 12, 21 and 32 are the pending independent claims. Claims 13, 29, 33 and 34 are dependent from independent claim 12, and claims 35-38 are dependent from independent claim 21.

A copy of all the rejected claims 12, 13, 21, 29 and 32-38, i.e., the claims involved in the appeal, is attached as a Claims Appendix, pursuant to Rule 41.37(c)(1)(viii).

(4) STATUS OF THE AMENDMENTS

A response to the final rejection of February 18, 2010 has not been filed.

(5) SUMMARY OF CLAIMED SUBJECT MATTER

Pursuant to 37 CFR § 41.37(c)(1)(v), the following is a concise explanation of the subject matter defined in each of the independent claims (i.e., independent claims 12, 21 and 32) involved in the appeal, which shall refer to the specification by page and line number, and to the drawing, if any, by reference characters.

Claims 12, 21 and 32 are the only independent claims of the claims on appeal.

Independent claims 12, 21 and 32 define methods of reducing apolipoprotein-B levels in the vascular system without reducing LDL-cholesterol levels in an individual in need thereof. See lines 1-2 of each of independent claims 12, 21 and 32; and the sentence spanning pages 3-4 of the specification.

The methods of independent claims 12, 21 and 32 include simultaneously administering azithromycin and acetylsalicylic acid to the individual, wherein the individual has hyperlipidemia. See lines 3-4 of independent claims 12 and 21 and lines 3-5 and 9 of independent claim 32; page 1, line 31 through page 2, line 3, page 2, lines 19-24, page 2, lines 26-28, and page 3, lines 1-2, of the specification. The methods of independent claims 12, 21 and 32 require reduction in apolipoprotein-B levels in the vascular system without reducing LDL-cholesterol levels in the treated individual. See 4-6 of independent claim 12, lines 4-7 of independent claim 21 and lines 4-6 of independent claim 32, and page 6, lines 4-24, of the specification.

Independent claim 32 additionally requires determination of levels of apolipoprotein-B and LDL-cholesterol in the vascular system of said individual following the required administration. See lines 7-8 of independent claim 32 and, for example, page 4, lines 13-16 of the specification.

Support for the details of dependent claims 29 and 36 may be found, for example, on page 3, of the specification in the paragraph spanning lines 16-21.

Support for the details of dependent claims 13 and 35 may be found, for example, on page 3, lines 23-24 of the specification as well as the Clinical Examples described on pages 11-13 of the specification..

Support for the details of dependent claims 33 and 37 may be found, for example, on page 4, lines 13-16 of the specification.

Support for the details of dependent claims 34 and 38 may be found, for example, on page 5, lines 7-10 of the specification.

(6) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The following ground of rejection are presented for review:

Whether the invention of claims 12, 13, 21, 29 and 32-38 would have been obvious from the combined teachings of Petyaev (WO 93/017992) in view of Ruggeni et al (U.S. Patent No. 6,369,071), as defined by 35 U.S.C. § 103.

(7) ARGUMENT

The methods of claims 12, 13, 21, 29 and 32-38 would not have been obvious from the combined teachings of Petyaev (WO 93/017992) in view of Ruggeni et al (U.S. Patent No. 6,369,071), and the rejection of claims 12, 13, 21, 29 and 32-38 under 35 U.S.C. § 103 over the cited combination of art should be reversed. Consideration of the following in this regard is requested.

The Examiner is understood to rely on Petyaev for a treatment of atherosclerosis by administration of azithromycin and a metal chelator, such as aspirin. See page 2 of the Office Action dated February 18, 2010. The Examiner acknowledges that Petyaev fails to teach a method of reducing apolipoprotein-B (apoB) levels in the vascular system. See page 2 of the Office Action dated February 12, 2009. The Examiner relies on Ruggeri to

> "disclose that a patient in need of apolipoprotein-B secretion inhibition is a patient having a disease condition in which apolipoprotein-B plays a role in the disease or condition such a patients having or are at risk of having atherosclerosis, hyperlipidemia and hypercholesterol." Id.

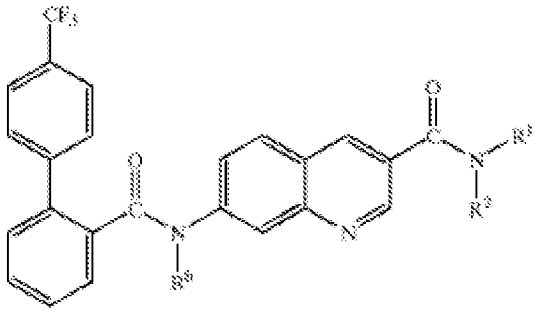
The Examiner concludes from the combination of references that it allegedly would have been obvious to have administered the combination of azithromycin and a metal chelator of Petyaev to patients in need of reduction of apolipoprotein "since such patients having or are at risk of having atherosclerosis are in need of such

treatment." See page 3 of the Office Action dated February 12, 2009. The Examiner has further asserted on page 3 of the Office Action of February 18, 2010 that

> "a person having ordinary skill in the art ... would have been motivated to treat individuals having hypercholesterolemia with a combination of azithromycin and acetylsalicylic acid disclosed by Petyev. The reduction of apo-B levels in the absence of reduction of LDL would have been inherent in such an administration."

The applicants note that Petyaev teaches, in part, a treatment of atherosclerosis by administering azithromycin and a metal chelator. The mechanism of the treatment described in Petyaev however is a reduction in lipoprotein peroxidation by administering the combination of azithromycin and a metal chelator. As admitted by the Examiner, there is no disclosure in Petyaev of reducing apoB levels. There is no suggestion in Petyaev of reducing apoB levels by administering azithromycin and a metal chelator.

As noted by the Examiner, Ruggeri describes a inhibition of apoB secretion can be useful to treat atherosclerosis. Ruggei teaches the use of compounds of the following structure to inhibit the secretion of apoB and thereby treat a number of diseases including atherosclerosis:



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Ruggeri also teaches that inhibition of apoB secretion "typically results in the lowering of plasma concentrations of compounds that contain apoB", such as LDL. See column 1, lines 51-54 and column 1, lines 31-33 of Ruggeri. Ruggeri further teaches that reduction in LDL levels has been used as a surrogate for reduction of apoB levels. See column 3, lines 10-65 of Ruggeri.

One of ordinary skill in the art will understand from Petyaev and Ruggeri that atherosclerosis may be treated by reducing lipid peroxidation (Petyaev) and/or by reducing secretion of apoB (Ruggeri). There is no suggestion in the art however that every treatment of atherosclerosis will necessarily involve a reduction in apoB levels, as appears to be the basis of the Examiner's obviousness rejection.

Moreover, the presently claimed invention defines methods whereby apoB levels in the vascular system are reduced without reducing LDL-cholesterol levels. The claimed methods are therefore contrary of Ruggeri which teaches that reduction in apoB secretion would result in a decrease of LDL and other lipoproteins that contain apoB.

Further, the Examiner's most recent assertion that "reduction of apo-B levels in the absence of reduction of LDL would have been inherent in such an administration" can not be the basis of a *prima facie* case of obviousness. The Examiner's reliance on an alleged or uncertain characteristic of the cited art (i.e., reduction of apo-B levels in the absence of reduction of LDL) can not be the basis of a *prima facie* case of obviousness.

Specifically, the Court has explained in In re Rijckaert, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993), for example, the following with regard to inherency and obviousness:

> The mere fact that a certain thing may result from a given set of circumstances is not sufficient [to establish inherency.]" In re Oelrich , 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981) (citations omitted) (emphasis added). "That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." In re Spormann, 363 F.2d 444, 448, 150 USPQ 449, 452 (CCPA 1966). Such a retrospective view of inherency is not a substitute for some teaching or suggestion supporting an obviousness rejection. See In re Newell, 891 F.2d 899, 901, 13 USPQ2d 1248, 1250 (Fed.Cir. 1989).

The Examiner's unfounded interpretation of the result of administration from the combination of cited art as a possible inherent feature which is not necessarily known from study of the cited art is not sufficient to establish obviousness of a feature of the claimed invention. As stated by the Court, obviousness cannot be

predicated on what is unknown. The claimed invention would not have been obvious from the combination of cited art.

For reasons including those set forth above and of record, the Board is respectfully requested to reverse the Section 103 rejection of claims 12, 13, 21, 29 and 32-38 over the combination of Petyaev (WO 93/017992) and Ruggeni et al (U.S. Patent No. 6,369,071).

Reversal of the 35 U.S.C. § 103, rejection of claims 12, 13, 21, 29 and 32-38 is requested.

The claims are submitted to be in condition for allowance and Reversal of the final rejection is requested.

Respectfully submitted,

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(8) CLAIMS APPENDIX

12. A method for reducing apolipoprotein-B levels in the vascular system without reducing LDL-cholesterol levels in an individual in need thereof comprising simultaneously administering azithromycin and acetylsalicylic acid to the individual, wherein the individual has hyperlipidemia, and said apolipoprotein-B levels in the vascular system of the individual are reduced without reducing said LDL-cholesterol levels in the individual.

13. A method according to claim 12 wherein the total level of cholesterol is reduced in the vascular system of the individual.

21. A method for reducing apolipoprotein-B levels in the vascular system without reducing LDL-cholesterol levels in an individual in need thereof comprising simultaneously administering azithromycin and acetylsalicylic acid to the individual, wherein the individual has hyperlipidemia; wherein said azithromycin and said acetylsalicylic acid are administered to the individual in an amount sufficient to reduce apolipoprotein-B levels in the vascular system without reducing LDL-cholesterol levels in said individual.

29. A method according to clam 12 wherein the individual does not have an atherosclerotic condition.

32. A method for reducing apolipoprotein-B levels in the vascular system without reducing LDL-cholesterol levels in an individual in need thereof comprising;

simultaneously administering azithromycin and aspirin to the individual, wherein said azithromycin and said acetylsalicylic acid are administered to the individual in an amount sufficient to reduce apolipoprotein-B levels in the vascular system without reducing LDL-cholesterol levels in said individual; and,

determining levels of apolipoprotein-B and LDL-cholesterol in the vascular system of said individual following said administration,

wherein the individual has hyperlipidemia.

33. A method according to claim 12 comprising determining the level of apolipoprotein-B and LDL-cholesterol in the vascular system of said individual following said administration.

34. A method according to claim 12 comprising determining the reduction in apolipoprotein-B levels and the lack of reduction in LDL-cholesterol levels in the vascular system of said individual, following said administration.

35. A method according to claim 21 wherein the total level of cholesterol is reduced in the vascular system of the individual.

36. A method according to clam 21 wherein the individual does not have an atherosclerotic condition.

37. A method according to claim 21 comprising determining the level of apolipoprotein-B and LDL-cholesterol in the vascular system of said individual following said administration.

38. A method according to claim 21 comprising determining the reduction in apolipoprotein-B levels and the lack of reduction in LDL-cholesterol levels in the vascular system of said individual, following said administration.

(9) EVIDENCE APPENDIX

Attached:

NONE

(10) RELATED PROCEEDINGS APPENDIX

Attached:

NONE